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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/185,243	11/03/1998	TOM TSANG	15907-0016	5192

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EXAMINER

PRIEBE, SCOTT DAVID

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 05/08/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/185,243

Applicant(s)
Tsang et al.

Examiner
Scott D. Priebe, Ph.D.

Art Unit
1632



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Mar 4, 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 48-75 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 48-75 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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DETAILED ACTION

The amendment filed 3/4/03 has been entered. Claims 1, 5, 9-18, 20-26, 33, 35-39 and 43-47 have been cancelled. Claims 48-75 have been added and are pending.

Specification

The declaration under 37 CFR 1.132 filed 3/4/03 is sufficient to overcome the objection to the specification under 35 USC 132.

Claim Rejections - 35 USC § 112

Claims 48-75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 48 and 56 recite “inducible promoter operably linked to a transactivating factor.” There is no support in the original specification for this limitation. The original specification describes operably linking the promoter to a polynucleotide (gene) encoding a transactivating factor, not to the transactivating factor itself. This appears to have been an inadvertent error in drafting the claims.

Claims 48, 50-56, and 58-75 are directed to an expression construct comprising an HIV-2 promoter and “an inducible promoter operably linked to a transactivating factor” (presumed to

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mean a polynucleotide encoding the transactivating factor). The claims embrace any transactivating factor able to activate transcription from an HIV-2 promoter. This broadening of the claimed embodiments of the invention where the transactivator may be any such factor which binds to and activates transcription from the HIV-2 promoter is not supported in the original specification. The original specification describes embodiments wherein the transactivator is tat when the second promoter is the HIV-1 or HIV-2 promoter (page 32, pages 34-35, original claims 9 and 43). The original specification does not mention or even allude to any transactivator other than tat when the HIV-2 promoter is part of the construct. There is no evidence of record indicating that applicant had contemplated any transactivator other than tat when the promoter linked to the "selected polynucleotide" is the HIV-2 promoter. It is suggested that claims 48 and 56 be amended to limit the "transactivating factor" to tat specifically, and that claims 49 and 57 be cancelled.

Applicant's arguments filed 3/4/03 have been fully considered but they are not persuasive. Applicant argues that it was recognized in the art that there were other proteins which could activate an HIV promoter. However, whether this is true or not, the issue is not whether others were aware of potential alternatives to tat, but whether the specification describes such alternatives as being part of the disclosed invention. The specification does not even hint at using transactivators other than tat for use with an HIV promoter, much less provide teachings directing one of skill to use myb, CMV IE-2 protein, herpesvirus ORF-1, etc. Applicant does not

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indicate where the instant specification directs one of skill to transactivators other than tat for the HIV-2 promoter.

Claims 56-67 are rejected and claim 47 is rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office action of 6/26/00 as applied to claims 1-15 and 17-38, because the specification while being enabling for methods of using the recited expression construct to effect expression of a selected polynucleotide in a mammalian cell *in vitro*, does not reasonably provide enablement for a method of using the expression construct *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

New claims 56-67 limit the previously claimed invention to embodiments wherein the promoter linked to the "selected polynucleotide" is an HIV-2 promoter. The claimed method can be carried out either *in vitro* or *in vivo*. With respect to embodiments carried out *in vivo*, the only use taught in the specification is for therapy. Those parts of the grounds of rejection set forth in the Office action of 6/26/00 which apply to the new claims are those dealing with gene therapy, but not with the scope of heat shock promoter.

Applicant's arguments filed 3/4/03 have been fully considered but they are not persuasive. Applicant argues that the specification discloses other uses than therapy, pointing to pages 3, last para.; page 14, first para.; page 25, last para.; page 58; and page 69. However, page 3, last para., merely states that the method is for effecting transgene expression in mammalian cells, without

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reference to where those cells are; and page 14, first para. merely teaches that heat shock promoters are the preferred inducible promoter for mammalian cells, and mentions therapeutic uses. Page 25 describes how to identify anti-sense polynucleotides to be “encoded” by the “selected polynucleotide”, it does not describe a use for the claimed method in such a process. The disclosure beginning of page 58, i.e. Example 1, is not directed to *in vivo* use, as suggested by Applicant, but to use in cultured cells; and is not directed to the study of reporter gene expression as suggested, but describes using reporter genes to assess the performance of the claimed expression constructs. Example 4, page 69 makes no mention of using the claimed method *in vivo* to assess potential therapeutic genes, as suggested by Applicant. Rather it describes a prophetic example for assessing the claimed method as a therapy, which use constitutes investigation on the invention rather than using the invention as a research tool.

Conclusion

Limitation of the claims to an HIV-2 promoter precludes rejection over Bromley et al., either alone or in view of other prior art. Bromley indicates that the role of the inducible promoter in this art is to provide little or no expression in the absence of inducer, and high expression in the presence of inducer, i.e. little expression when not desired and high expression when desired. Bromley used an HIV-1 promoter (described simply as HIV promoter), and does not suggest using the HIV-2 promoter. The results shown in the specification, Tables 4-6, show that even in the uninduced state, the construct made with the HIV-2 promoter yields higher

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expression than does the HIV-1 promoter following induction or the CMV promoter, and little induction is observed using the HIV-2 promoter. As indicated in Brady et al. (Proc. Natl. Acad. Sci. USA 91: 365-369, 1994, e.g. abstract), it was known in the art that the HIV-2 promoter “has a considerable level of basal expression.” Thus the results disclosed in the specification are not entirely unexpected. These results and the knowledge in the art that the HIV-2 promoter “has a considerable level of basal expression” would suggest to one of skill in the art that the HIV-2 promoter would be a poor substitute for the HIV-1 promoter in the vectors of Bromley, which would be motivation not to use it.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

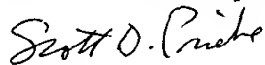
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX numbers are (703) 308-4242 or (703) 305-3014 for any type of communication. In addition, FAX numbers for a computer server system using RightFAX are also available for communications before final rejection, (703) 872-9306, and for communications after final rejection, (703) 872-9307, which will generate a return receipt. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 8 AM to 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Scott D. Priebe, Ph.D.
Primary Examiner
Technology Center 1600
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